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Retrospective Analysis of 1998 Patients Diagnosed with Brain Death between 2011 and 2019 in Turkey

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Abstract

Background Organ transplantation reduces mortality and morbidity in patients with end-stage organ failure. The number of living organ donations is not enough to meet the current organ transplantation need; therefore, there is an urgent need for organ donation from cadavers. We aimed to determine the organ donation rates and reveal the obstacles against donation.

Methods This study is designed as a retrospective multicenter study consisting of eight university hospitals, three training and research hospitals, 26 state hospitals, and 74 private hospitals in nine provinces in Turkey. A total of 1,998 patients diagnosed with brain death between January 2011 to April 2019 were examined through the electronic medical records data system.

Results Median patient age was 38 (IQR: 19–57), and 1,275 (63.8%) patients were male. The median time between the intensive care unit admission and brain death diagnosis was 56 (IQR:2–131) hours. The most commonly used confirmatory diagnostic test was computed tomography in 216 (30.8%) patients, and the most common cause of brain death was intraparenchymal hemorrhage with 617 (30.9%) patients. A total of 1,646 (82.4%) families refused to permit organ donation. The most common reasons for refusal were family disagreement (68%), social/relative pressure (24%), and religious beliefs (8%).

Conclusions Many families refuse permission for organ donation; some of the provinces included in this study experienced years of exceptionally high refusal rates.

Keywords
- brain death
- organ transplantation
- donation
- intensive care
- Turkey

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Introduction

Brain death (BD) is defined as the irreversible loss of all brain functions, including the brain stem.[1] International guidelines provide acceptance criteria for BD diagnosis and organ donation management procedures.[2] Although there is a clear consensus on the definition of BD, there may be differences between guideline recommendations and current practices. Furthermore, practices vary at the national and international levels regarding additional tests and organ donation management.[3–5] Access to donated organs through organ transplantation is a source of hope for many patients suffering from end-stage organ failure (potential organ recipients), and patients diagnosed with BD are strong candidates for cadaveric organ donation (potential organ donors). Despite the increased number of potential organ recipients, the number of potential living organ donors remains low, resulting in insufficiency to meet the needs of the potential organ recipients.[6,7] Increasing the number of cadaveric organ donations is an important subject.[8] To accomplish an increase in the number of cadaveric donations, we must first fully understand the clinical practice, donation rates, and donation barriers. In Turkey, the National Organ Transplant Coordination Centre, which operates under the supervision of the Turkish Ministry of Health, is responsible for managing both BD diagnosis and organ donation. In this current study, we examined the practice of BD diagnosis, cadaveric organ donation rates, and organ donation barriers within the territory of the Adana regional coordination center, one of nine regional coordination centers that consist of the National Organ Transplant Coordination Centre.

Materials and Methods

This study covered the period between January 2011 and April 2019. We used the data obtained from electronic records held and maintained by the Adana regional coordination center. These records included organ transplant data from eight university hospitals, three training and research hospitals, 26 state hospitals, and 74 private hospitals affiliated with the Adana regional coordination center. Study evaluation was undertaken by local coordination centers, with study contacts officially established through the provincial directorate of health. Specifically, the Adana regional coordination center obtained permission from the National Organ Transplant Coordination Centre to perform the study. The study sample consisted of all patients diagnosed with BD in the hospitals affiliated with the Adana regional coordination center. In addition, hardcopy patient files were examined for the missing data that were not recorded in the electronic records; any such missing data was manually added to the electronic records.

A total of 2,005 patient files were examined, seven patients were excluded due to missing data. Therefore, the final study sample consisted of 1,998 patients.

Patients with a Glasgow coma scale three were included to diagnose BD. Cranial imaging was performed for all patients, and the cause of the coma was documented radiologically.

It was ensured that the selected patients did not have severe hemodynamic disorders, were not under the influence of sedation, and had no infectious agents such as sepsis. In other words, metabolic conditions that could be confused with coma were ruled out. The following examinations were performed to evaluate brain stem reflexes: (1) pupil reflexes, (2) oculocephalic and vestibulo-ocular reflexes, (3) absence of corneal reflexes, (4) pharyngeal and tracheal reflexes, (5) absence of spontaneous respiratory effort and apnea test. The apnea test was performed when prerequisites met normothermia, normotension, and normovolaemia. In patients who met the apnea test criteria, $PaCO_2$ should be 35 to 45 mm Hg, and PaO2 should be above 200 mm Hg with the appropriate mechanical ventilation approach to the patient. After these conditions are met, the patient should be disconnected from mechanical respiratory support and given intratracheal oxygen. At the end of the test, the apnea test was considered positive if the PaCO2 was $\geq$60 mm Hg and/or the $PaCO^2$ had increased by 20 mm Hg or more from baseline, with no spontaneous breathing. An apnea test was performed in all patients for brain stem functions. In those whose apnea test results could not be determined clearly, cerebral blood flow was measured by angiography (additional test).[8–10] Physicians diagnosing BD were organ transplant coordinators. Since the diagnosis certification was given to only a limited number of people, some doctors who decided on BD diagnosis did not have the certificate, but all the nurses who performed the test had the certificate.

According to the laws in our country, a diagnosis of BD is decided by two physicians, one of whom is a neurologist or neurosurgeon and the other an anesthesiologist or intensive care specialist, in accordance with the rules of evidence-based medicine.

Families were interviewed in a separate room by a group of physicians who were organ transplant coordinators, a psychologist, and a religious officer working in the hospital. Religious groups were not questioned.[2]

The study was retrospective. Since organ donation awareness studies were conducted in these provinces at least twice a year, we could only document the existing ones. The rejection rate was different in different provinces, which may depend on the coordinators. Also, there have been coordinator changes over the years. Seminars were held to improve organ donation.

BD diagnostic criteria are no different between provinces. A confirmatory test was performed in cases whose apnea test was not negative but occasionally suspected (in additional conditions such as chronic obstructive disease and chest deformity that may increase the CO_2 level). Those who were not clearly positive were considered negative, and the confirmatory test results were considered to diagnose BD.

Statistical Analysis

Statistical analysis was performed with the Statistical Package for Social Sciences (SPSS) for Windows v. 22.0 (IBM Corp., Armonk, New York, United States). Median, interquartile range (IQR), and percentages were calculated as descriptive statistics. In addition, qualitative data were compared with

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Pearson's Chi-square test. A p-value of <0.05 was considered statistically significant.

Ethical Approval

Ethics approval was obtained from the ethics committee of Katip Celebi University (no:357).

Results

The median age of patients diagnosed with BD was 38 (IQR: 19–57) years. The median time between intensive care unit (ICU) admission and BD diagnosis was 56 (IQR:2–131) hours. The apnea test was positive in 1,741 (87.1%) patients, and a confirmatory test was used in 702 (35.1% of the study population) patients. The three most commonly used confirmatory tests were CT angiography in 216 patients (30.8% of the study population in which ancillary diagnosis was performed), magnetic resonance angiography in 197 patients (28.1%), and Doppler ultrasonography (USG) in 154 patients (21.9%). The most common cause of BD was intraparenchymal hemorrhage (617 patients, 30.9%), followed by subarachnoid hemorrhage (513 patients, 25.7%). While 352 (17.6%) of the patients' family members consented to organ donation after BD diagnosis, 1,646 (82.4%) did not give consent (►**Table 1**). BD etiology remained similar throughout the study period (►**Fig. 1**), and there were no significant changes in the time between ICU admission and BD diagnosis ($p = 0.847$). While BD population rates were constant throughout the study period in some geographic regions, they underwent sudden changes in others (►**Fig. 2**). Finally, the number of organ donations was as low as zero when expressed as a population proportion in some provincial centers (►**Fig. 3**).

Discussion

The most concerning finding of our study is the low number of organ donations. Organ donation was refused by the families of 1,646 (82.4%) potential organ donors, a higher refusal rate than the average rate in Turkey overall. In 2017, 72.9% of families in Turkey refused to permit cadaveric organ donations. That ratio was 25% in Greece, 29.5% in Romania, and 62.3% in Saudi Arabia.[11] Indeed, family refusal is the most critical obstacle to cadaveric organ donation. In addition, while public opinion polls in Turkey indicate that 75% of the population is willing to donate their relatives' organs, this rate decreases to 24% in actual cases.[12] Families stated the following reasons for refusing to permit organ donations mainly as follows: family disagreement over donation decision (1,119 patients, 68%), social/relative pressure (395 patients, 24%), and religious beliefs (132 patients, 8%). A further investigation of the underlying causes of the family disagreements over donation decisions revealed that in 79% of these cases, some family members believed that the patient had a heartbeat and, therefore, still had a life chance unless organ donation was not permitted. In 21% of cases where the family refused permission for organ donation, the family believed that the patient had not expressed a desire to

Table 1 Demographic data

Variables	
Age: years median (IQR)	38 (19–57)
Gender *n* (%)	
Male	1,275 (63.8)
Female	723 (36.2)
Time between ICU admission and brain death: hours median (IQR)	56 (2–131)
Number of patients by city: *n* (%)	
Adana	588 (29.4)
Gaziantep	425 (21.3)
Mersin	387 (19.4)
Hatay	243 (12.2)
Maraş	219 (11.0)
Kayseri	40 (2.0)
Osmaniye	40 (2.0)
Kilis	31 (1.6)
Niğde	25 (1.3)
Apnea test: *n* (%)	
Positive	1,741 (87.1)
Negative	257 (12.9)
Confirmatory tests: *n* (%)	
CT angiography	216 (30.8)
Doppler USG	154 (21.9)
MR angiography	197 (28.1)
DSA	56 (8.0)
EEG	55 (7.8)
Scintigraphy	24 (3.4)
Diagnosis: *n* (%)	
Intraparenchymal hemorrhage	617 (30.9)
SAH	513 (25.7)
Other	397 (19.9)
Hypoxic brain injury	211 (10.6)
Ischemia	180 (9.0)
Subdural hemorrhage	52 (2.6)
Epidural hemorrhage	28 (1.4)
The family decision for organ donation: *n* (%)	
Consent	352 (17.6)
Refusal	1,646 (82.4)
Family refusal reason: *n* (%)	
Family conflict	1,119 (68)
Social/relative pressure	395 (24)
Religious beliefs	131 (8)

Abbreviations: CT, computed tomography; DSA, digital subtraction angiography; EEG, electroencephalography; IQR, interquartile range; MR, magnetic resonance; SAH, subarachnoid hemorrhage; USG, ultrasonography.

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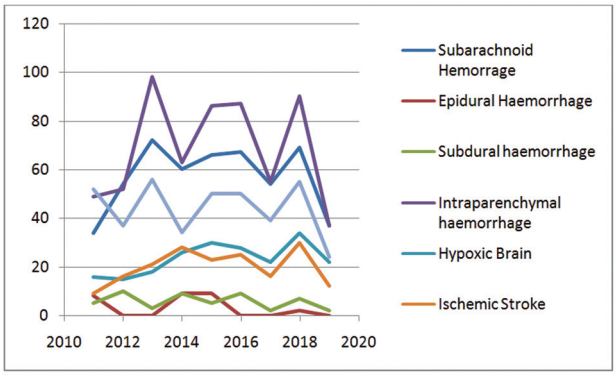

Fig. 1 Brain death etiology during the study period.

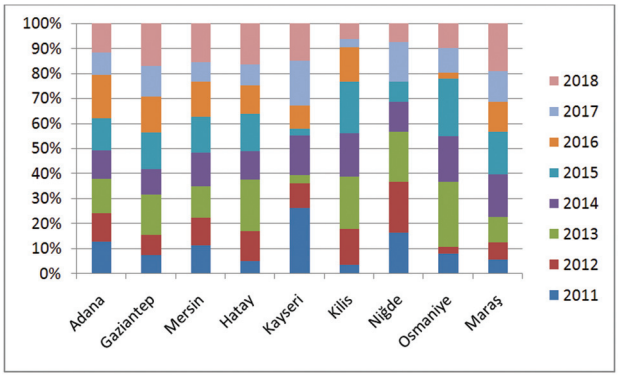

Fig. 2 The ratio of number of brain death per province populations by years.

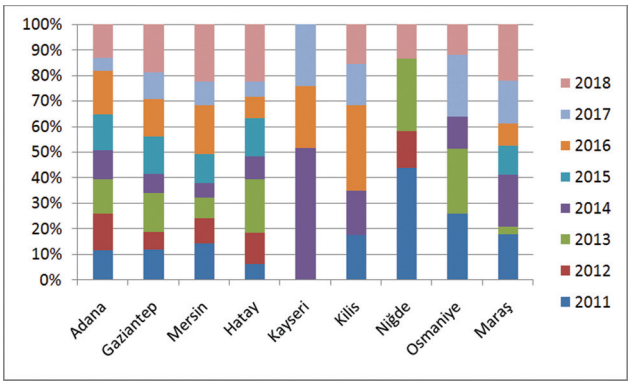

Fig. 3 The ratio of the number of the donor consents per the province populations by years.

donate their organs while alive and, therefore, permitting donation would not honor the patient's living wishes. These findings highlight the need for proper and adequate family information about organ donation to increase the donation rates in Turkey. The global incidence of people who have been adequately informed about organ donation ranges between 60 and 85%, with variations being mainly due to different cultures and religious beliefs.[13] For example, while 88% of the population in New York is informed about organ donation, only 60% are informed in Turkey.[14,15] In a study by Can and Hovardaoglu, the families of 101 patients diagnosed with BD were interviewed to determine the factors that affected their donation decisions; 65 of the study families permitted organ donation, while 36 did not. Of the 65 families who have given consent for organ donation, 75.9% agreed because they considered it gave hope and contributed to extending another person's life. A further 24.1% of the families who gave organ donation permission stated that they felt like their deceased relative would have agreed with their decision. Interestingly, only 9.2% of the patients whose families gave organ donation permission held an organ donation card. These results suggest that donation rates might increase if the general population has a positive attitude against organ donation and if individuals discuss their idea about donation with their families during their healthy lives. In this context, we expect that providing accurate information to the general population about organ donation will positively affect families' decisions about organ donation after death.[16] Previous studies demonstrated that family members take the opinion of their deceased relative into account when deciding whether to permit organ donation.[16]

Therefore, it is reasonable to expect that having a positive attitude to organ donation in life will affect family decisions on organ donation in death. Another important factor that influences donation decisions is communication between health care providers and families of the deceased. In the study by Can and Hovardaoglu, 21.7% of the families who refused to permit organ donation stated that their reason for refusal was the health care professional's negative attitude toward families.[11] Sarıtaş et al interviewed 163 ICU health care professionals to investigate the professional's considerations about the main barriers to organ donation. The authors concluded that the main barrier to organ donation was incomplete and unsatisfactory explanations of BD by health care professionals to patients' families. Sarıtaş et al reported that most health care professionals in their study lacked the confidence to make a firm BD diagnosis, leaving them unable to make the necessary clinical decisions. The health care professionals also felt that the BD diagnosis protocols provided by the Turkish Ministry of Health were unhelpful and in need of improvement if they were to contribute to improvements in organ donation rates.[17] The lack of official guidance on BD diagnosis may have contributed to the below-average organ donation rates in the present study. While the number of BD diagnoses was stable over time for some cities in our study, for others, it was not; for example, there was an apparent and unexplained decrease in the number of BD diagnoses made in the years 2013 and 2015 in Kayseri. We expect that improved procedures and regulations regarding BD would improve public understanding of BD and, in turn, would improve organ donation rates. While organ donation coordinators, who have a key role in improving donation rates, are assigned by the Ministry of Health in Turkey, Sarıtaş et al reported that most health care professionals thought that doctors should take the role of organ donation coordinators.[17] Kayseri, a metropolitan city with over one million, had a high cadaveric organ donation rate in 2014, but no donations in 2012, 2013, or 2015 (►**Fig. 3**) were observed. Organ donation decisions are

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strongly influenced not only by rules and regulations but also by the opinions of the organ donation coordinator, who must have a positive attitude toward a donation to maximize the chances of donor families permitting to donate.

A review of 248 studies published between 1985 and 2013 period revealed that, in general, doctors and nurses had a positive attitude toward organ donation and transplantation, but they were less positive when the potential organ donor was a member of their own family.[18] In a survey of 309 health care professionals working in 27 dialysis centers in Turkey, 59.7% of the study participants expressed a fear of unlawful organ harvesting and transplanting donated organs to incompatible organ recipients.[19] Even if the families are appropriately informed about organ donation with a positive attitude by health care professionals, inadequate communication with donor family members adversely affects the final donation decision. Studies regarding the attitudes of donor family members reveal the importance of effective communication between health care professionals and donor family members when families must decide whether to permit to donate.[20,21] In the present study, we found that social/relative pressure prevailed over religious pressure when families considered their decision to allow organ donation. Indeed, 395 (24%) of the donor family members who did not give permission to donate stated that social/relative pressure was the reason for their decision, and they were worried that their relatives might consider that they had failed their deceased family member if they had given permission. Although religious beliefs rarely cause family members to refuse donation permission, the effects of religious beliefs cannot be entirely ignored. Specifically, when religious believers understand that their church supports organ donation and transplantation, they are more likely to have a positive personal attitude to organ donation and transplantation.[22–24] Although the data used in the present study included information about why families did not permit to donate, it did not include complementary information about why the rest of the families had given consent to donate. This imbalance in the collected data was perhaps due to an intentional attempt to avoid changing their mind by questioning the families too profoundly, who had already agreed to donate.

We found that BD was, in general terms, diagnosed according to the current guidelines, and the most common cause was intracranial hemorrhage which was similar to the literature findings whereby no etiological changes have been observed throughout our study.[2,3] The mean time between ICU admission and BD diagnosis (median 56[IQR:2–131] hours) was longer than a comparable study conducted in Spain, in which BD was diagnosed within 24 hours of ICU admission.[25] We believe that this relatively long diagnosis timeframe was due to the context of the working conditions in Turkey, where ICU staff shortages are commonplace.[26] Confirmatory tests were used in 702 (35.1%) patients, despite the apnea tests being negative in 257 (12.9%) patients; these confirmatory tests may have been used to prove the BD diagnosis further and to shorten the time to the final diagnosis.

Study Limitations

Its retrospective design prevented the investigation of data that was not recorded at the time of the patient's death. Specifically, it was impossible to investigate why some families have permitted to donate, complementary to why other families did not permit to donate.

ICU bed capacity is limited in Turkey, resulting in potential organ donors not being admitted to the ICU and, therefore, never evaluated for donation by donor coordinators.

Conclusions

We concluded that cadaveric organ donation rates are meager in Turkey. The main barriers to organ donation are family conflicts, inadequate information regarding BD, and social/relative pressure on family members when deciding whether to permit them to donate. Furthermore, some Turkish provinces had sudden and unexplained decreases in BD diagnosis rates; these decreases are a cause for concern and must be addressed by the Ministry of Health.

Conflict of Interest
None declared.

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